



The impact of ambient temperature on acute myocardial infarction admissions in Tehran, Iran

Rasool Mohammadi^{a,b}, Hamid Soori^c, Abbas Alipour^d, Ehsan Bitaraf^e, Soheila Khodakarim^{f,*}

^a Assistant Professor of Epidemiology, School of Public Health, Lorestan University of Medical Sciences, Khorramabad, Iran

^b Nutritional Health Research Center, Health and Nutritional Department, Lorestan University of Medical sciences, Khorramabad, Iran

^c Professor of Epidemiology, Safety Promotion and Injury Prevention Research Center, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran

^d Assistant Professor of Epidemiology, Department of Epidemiology, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran

^e IT Office, Ministry of Health & Medical Education, Tehran, Iran

^f Assistant professor of Biostatistics, Department of Epidemiology, School of Paramedical Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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ABSTRACT

While the effect of temperature on risk of cardiovascular events is well documented, few studies report evidence from the Middle East. In this study, we investigate the short-term effect of ambient temperature on admissions for acute myocardial infarction (AMI) in Tehran, Iran. We used a case-crossover design combined with a distributed lag non-linear model to examine nonlinear and delayed associations between ambient temperature and AMI admissions from 2013 to 2016. We also examined hot and cold effects on AMI admission by gender and age categories (≤ 65 years old and > 65 years old). Both hot and cold temperatures increased the risk of AMI admissions. Effects of high temperature appeared immediately on the current day and lasted for 3 days, whereas cold effects became apparent after 2 days and persisted for about 8 days. The early acute increase in risk associated with high temperature was followed by a deficit, thus suggesting evidence of a harvesting effect. In additions, males and those aged ≤ 65 years old were more vulnerable to high temperatures.

1. Introduction

In recent years and as a response to global climate change, investigating the adverse effects of meteorological factors on human health has gained particular interest. Climate change is expected to raise the frequency and intensity of extreme temperatures (heat waves and cold spells) worldwide (Guo et al., 2016; Madrigano et al., 2013). Extreme temperatures have been found to have significant harmful effects on human health. Ambient temperature has been linked to an increased risk of childhood pneumonia (Miao et al., 2017; Zeng et al., 2017). Several epidemiological studies have reported a nonlinear U, V, or J-shaped association between ambient temperature and mortality, which indicated that both high and low temperatures have adverse effects on mortality (Breitner et al., 2014; Ma et al., 2014; Baccini et al., 2008; Zhang et al., 2016).

Increased mortality during high and low temperature extremes has been shown to be mainly related to cardiovascular diseases (CVDs) (Knowlton et al., 2009; Braga et al., 2002; Bhaskaran et al., 2009), and similar nonlinear (U-, V-, or J-shaped) relationships between temperature and CVD mortality have been described (Breitner et al., 2014; Zhang et al., 2016; Huang et al., 2017). Among CVDs, the most likely

effect is on acute myocardial infarction (AMI), the leading cause of morbidity and mortality globally (Barnes et al., 2015; Kwon et al., 2015; White and Chew). Previous studies, mainly from developed countries, have reported that both cold and hot ambient temperature significantly increased the risk of AMI hospitalization (Wichmann et al., 2012b; Bhaskaran et al., 2010; Bhaskaran et al., 2012) and mortality (Dilaveris et al., 2006; Gasparrini et al., 2012). Bhaskaran et al. systematically reviewed studies specifically focusing on the effects of temperature on AMI and found that both hot and cold temperatures had adverse effects on the risk of AMI (Bhaskaran et al., 2009).

Importantly, temperature-related health outcomes are greatly affected by geographic locations, population characteristics, and the type of climate at specific locations (Zhang et al., 2016; Guo et al., 2011, 2014). People in developing countries can be more sensitive to extreme temperatures than people in developed countries due to inadequate or nonexistent public health infrastructures and their restricted coping capacity (Zhang et al., 2016; McMichael et al., 2008). The Middle East is one of the areas that climate change has affected significantly. During the 20th century, temperatures in this region increased 0.4 °C per decade, which was much faster than the global rate. Moreover, a significant increase in the frequency and intensity of droughts and hot

* Corresponding author.

E-mail addresses: rasool.mehr2002@gmail.com (R. Mohammadi), lkhodakarim@gmail.com (S. Khodakarim).

weather conditions has been projected (Lelieveld et al., 2012). Iran is one of the largest countries in the Middle East, and it has been estimated that its average temperature will increase by 1.5–4.5 °C by 2100 due to climate change (Amiri and Eslamian, 2010; Khanjani, 2016). In a recent study of temperature fluctuations in Iran, Darand et al. reported that, for the period from 1962 to 2004, the frequency of extremely hot temperatures increased, whereas the frequency of extremely cold temperatures decreased (Darand et al., 2015).

Few studies have focused on the effects of ambient temperature on mortality and morbidity in Iran and, more generally, in the Middle East. El-Zein et al. examined the relationship between temperature and daily mortality in Greater Beirut and found a significant, V-shaped association (El-Zein et al., 2004). Khanjani et al. reported that cardiovascular and respiratory disease mortality in Kerman, Iran, was associated with decreases in temperature (Khanjani and Bahrampour, 2013).

To the best of our knowledge, no study to date has addressed the impact of ambient temperature on AMI morbidity in the Middle East. Therefore, the aim of this study is to investigate the short-term effect of temperature on AMI admissions in Tehran, Iran.

2. Materials and methods

2.1. Study area and population

Tehran is located at about 35°41'N latitude and 51°25'E longitude. It is situated 1178 m above sea level, and it has a semi-arid climate with continental climate characteristics and a Mediterranean climate precipitation pattern. Tehran's climate is largely determined by its geographic location, with the towering Alborz Mountains to its north and the central desert to the south. The city has four distinct seasons and can be generally characterized as mild in the spring and autumn, hot and dry in the summer, and cold and wet in the winter. With a population of about 9 million in 2015, Tehran is Iran's most populated city and is the second most populated city in Western Asia.

2.2. Data collection

In the present study, we extracted data on the daily counts of AMI admissions in Tehran from March 21, 2013, to March 19, 2016, from the Iranian Myocardial Infarction Registry (IMIR). Established in 2009 by the Office of Cardiovascular Diseases of the Iranian Ministry of Health and Medical Education, the IMIR is a patient-centric registry system that is compatible with the Iranian Electronic Health Record (locally called SEPAS). The data exchange protocol between the IMIR and SEPAS is based on the international standard ISO 13606, which enables patient encounters to be stored in a distributed national repository (Riazi et al., 2014).

The diagnostic groups in this study included all AMI admissions with a primary diagnosis coded I21 - I22 according to the International Classification of Diseases, 10th Revision. The daily weather data on maximum, mean, and minimum temperature and relative humidity during the study period were provided by the Islamic Republic of Iran Meteorological Organization in Tehran. To adjust for the potential confounding effects of air pollution (Guo et al., 2011; Miao et al., 2017), we collected 24-h averages of particulate matter < 10 μm in aerodynamic diameter (PM10) (μg/m³), sulfur dioxide (SO₂) (ppb), nitrogen dioxide (NO₂) (ppb), and ozone (O₃) (ppb) from the Iranian Department of Environment. These pollutants were averaged from 14 stations located in different parts of Tehran. Although during the study period there were no missing values for meteorological data, from March 3, 2016, to March 19, 2016, we had 17 days with no air pollution data; therefore, they were excluded from the analysis.

2.3. Statistical analysis

Previous studies have reported nonlinear and delayed effects of

temperature on cardiovascular outcomes (Turner et al., 2012); hence, we fitted time-stratified case-crossover design jointly with distributed lag nonlinear model (DLNM) to explore temperature's effect on AMI hospitalizations. The DLNM employs a cross-basis function to flexibly describe the nonlinear and the lagged effects simultaneously. The DLNM allows modelling of a bidimensional relationship in the dimensions of temperature and lag (Gasparrini et al., 2010). Time-stratified case-crossover design is a special case of a time series analysis and uses fixed and short-interval strata (e.g., calendar month) to control for seasonal variation and long-term trends (Guo et al., 2011, Lu and Zeger, 2007). Since a case-crossover design has limited ability to explore nonlinear effects, applying case-crossover design jointly with a DLNM model permits a more sophisticated assessment of the nonlinear and lagged effects of temperature on AMI admissions while adjusting for seasonal variation and long-term trends by design (Guo et al., 2011). To combine DLNM with the case-crossover design, we constructed a quasi-Poisson function that allows for overdispersion in daily AMI admissions:

$$Y_t \sim \text{Poisson}(\mu_t)$$

$$\begin{aligned} \text{Log}(\mu_t) = & \alpha + \beta T_{t,l} + ns(RH_t, 3) + ns(PM_{10t}, 3) + ns(SO_{2t}, 3) \\ & + ns(NO_{2t}, 3) + ns(O_{3t}, 3) + \lambda Strata_t + \gamma DOW_t \\ & + \omega \text{Holiday}_t \end{aligned}$$

Where t denotes the time (day) of observation; Y_t denotes observed daily AMI admissions on day t ; α is the intercept; $T_{t,l}$ represents matrices obtained by applying cross-basis function in the DLNM to mean daily temperature; β is vector of coefficients for $T_{t,l}$ and l indicate the lag days. $ns()$ represents natural cubic spline, RH_t represents the daily mean relative humidity on day t , and 3 is the degrees of freedom (df). $Strata$ is a categorical variable of the year and calendar month used to control for long-term trend and seasonality, and λ is a vector of coefficients. DOW_t is an indicator variable to control the day of the week on day t , and γ is a vector of coefficients. $Holiday_t$ refers to a binary variable that is "1" if day t was a holiday, and ω is the coefficient. To assess the nonlinear and lagged effect of ambient temperature on AMI admissions, a "natural cubic spline-natural cubic spline" DLNM using a 5 df natural cubic spline for temperature and a 4 df natural cubic spline for lag was used. The df for temperature and lag was chosen according to Akaike information criterion for quasi-Poisson models (Q-AIC) (Gasparrini et al., 2010, Peng et al., 2006). Spline knots of temperature were placed evenly across the temperature range to allow enough flexibility in the two ends of temperature distribution. The spline knots of lag were set at equal spaces in the log scale of lags [30]. Previous studies have shown that the effects of cold temperature could persist for weeks and that the effects of hot temperatures are usually short-term and immediate (Guo et al., 2011, 2014). Therefore, we set maximum lag up to 27 days to adequately model temperature's overall effect on AMI admission and to account for a possible harvesting effect (an initial rise in morbidity or mortality followed by a period of lower-than-expected morbidity or mortality) of hot temperatures (Guo et al., 2011, Armstrong, 2006). We controlled RH , PM_{10} , SO_2 , NO_2 , and O_3 concentrations as potential confounders of the association between temperature and AMI admission by using a natural cubic spline with 3 df based on previous studies (Guo et al., 2010, Yi and Chan, 2015, Yang et al., 2012). The median value of temperature measures (minimum, mean, and maximum temperature) during the study period was designated as the reference value to estimate the relative risks (RRs). For each temperature measure, a model using the above-mentioned steps was fitted. We used Q-AIC to appraise model fitting and determine the temperature index that best predicted AMI admission. Our initial analysis indicated that the mean temperature had the lowest Q-AIC and the largest RR values compared to the other two temperature measure. Therefore, only the results of mean temperature were reported.

Using estimates and standard errors from DLNM, we can obtain

graphs and statistical inference (Armstrong, 2006). Hence, we used a case-crossover design combined with DLNM to predict the effects and standard error at different combinations of temperature and lags. Three-dimensional diagrams were plotted to illustrate the RRs of association between temperature and AMI admission along both temperature and lags by comparing them with the median value of temperature. The cumulative effect of mean temperature on AMI admission over 0–3, 0–7, 0–14, 0–21, and 0–27 lag days was also estimated.

To evaluate the effects of high temperature on AMI admission, we calculated the RR associated with 95th percentiles of mean temperature (33.3 °C) relative to the 75th percentile of mean temperature (28.4 °C). Cold's effect on AMI admission was also evaluated by comparing the 5th percentiles of mean temperature (4.8 °C) with the 25th percentile of mean temperature. We also examined hot and cold effects on AMI admission by gender and age categories (≤ 65 years old and > 65 years old).

To check the robustness of our main findings, we conducted sensitivity analyses by changing the maximum lag (27) from 14 to 30 days. We also changed the window interval of the calendar month in the case-crossover design to 30, 28, and 21 and the df for relative humidity, PM₁₀, SO₂, NO₂, and O₃ from 4 to 7. We used AIC-Q to evaluate the model fitting. We regarded the model with lowest Q-AIC as the final model.

We used R software (version 3.2.5; R Foundation for Statistical Computing, Vienna, Austria) to perform the analyses. The “dlnm” package (version 2.3.2) was used to create the DLNM (Gasparrini, 2011). All statistical tests were two-sided, and p-values < 0.05 were considered statistically significant. The estimated RRs with corresponding 95% confidence intervals were presented.

3. Result

During the study period (March 21, 2013, through March 2, 2016), there were a total of 15,835 AMI admissions in Tehran. Of these, 11045 (69.7%) were male, and 10049 (63.5%) were ≤ 65 years. Table 1 shows the descriptive statistics for the daily weather variables and air pollutants during the study period. The average daily mean, maximum, and minimum temperature and relative humidity were 19.08 °C (range -0.89 – 36.5 °C), 23.13 °C (range 0.4 – 42.6 °C), 14.12 °C (range -7.6 – 32 °C), and 31.82% (range: 7.46%, 85.07%), respectively. The 24-h mean concentration of PM₁₀, NO₂, SO₂, and O₃ were 96.62 $\mu\text{g}/\text{m}^3$ (range 31.78–364.44), 36.69 ppb (range 15.49–67.27), 19.97 ppb (range 9.31–50.13), and 25.03 ppb (range 6.43–53.73), respectively.

Table 2 presents the Pearson correlation coefficients of weather variables and air pollution. Mean, maximum, and minimum temperature were positively correlated with each other and were negatively

associated with relative humidity. Three temperature measures had moderate negative correlation with NO₂, whereas mean and maximum temperature were positively correlated with O₃. There was no correlation between three temperature measures and PM₁₀. The concentrations of PM₁₀, SO₂, and O₃ were moderately associated with each other.

Fig. 1 shows the three-dimensional plot of the relationship between mean temperature and AMI admission along 27 lag days. The graphs revealed nonlinear relations between temperature and AMI admission, with higher deleterious effects at high temperatures. For example, extremely hot temperature (36.5 °C) increased the risk of AMI admission between lag 0 and lag 4, with the highest RR on the same day (lag 0). By contrast, cold effect appeared at about 5 °C and lag 3 that peaked approximately at lag 5 and then steadily declined. There was no association between extremely low temperature (-0.89) and AMI admission along 27 lag days.

Fig. 2 presents the estimated cumulative effects of mean temperature on AMI admission at lags 0–3, 0–14, and 0–27. The graph indicates nonlinear relationships between mean temperature and AMI admissions. The RR of AMI admission increased steadily when mean temperature was above median temperature (19.3 °C), with the largest RR at highest temperature. However, the cumulative effects of extremely hot temperature on AMI admission at lags 0–3 were lower than at lags 0–14 and 0–27; a statistically significant effect of extremely hot temperature was observed only at lags 0–3. Temperatures at below median had a protective effect on AMI admission at lags 0–3. Temperature's effects on AMI admission show a virtually identical pattern at lags 0–14 and lags 0–27. At lags 0–14 and lag 0–27, we found a non-significant increase in risk of AMI admission at about 4–10 °C.

Fig. 3 presents the estimated effects of high temperature (33.3 °C, 95th percentile of mean temperature) compared with the 75th percentile of mean temperature (28.4 °C) on AMI admissions by gender and age categories (≤ 65 years and > 65 years) over 27 days of lag. In the overall population, males, and people aged ≤ 65 years old, significant hot effect appeared immediately on the current day (lag 0) and disappeared after about 3 days. The early acute effect of high temperature on AMI admission in the overall population and those aged ≤ 65 years old was followed by deficits in AMI admission, which suggests the presence of a harvesting effect. For females and people aged > 65 years old, no significant increased risk of AMI was observed in the exposure to high temperatures.

The estimated effects of cold temperature on AMI admissions by gender and age categories over 27 days of lag were displayed in Fig. 4. In general, the effects of cold temperature on AMI admission in the overall population and in all subgroups revealed a similar pattern. In the overall population, males, and people aged ≤ 65 years old, significant cold effects appeared after a 2-day lag and remained elevated

Table 1
Descriptive statistics of daily AMI admissions, weather conditions and air pollutants in Tehran, Iran, 2013–2016.

Variable	Mean $\pm$ SD	Minimum	Percentile			Maximum
			25th	50th	75th	
Total AMI	14.69 $\pm$ 5.27	0	12	15	18	33
Male	10.25 $\pm$ 3.97	0	8	10	13	27
Female	4.44 $\pm$ 2.45	0	3	4	6	14
≤ 65 years	9.32 $\pm$ 3.81	0	7	9	12	24
> 65 years	5.37 $\pm$ 2.66	0	3	5	7	14
Temperature (°C)						
Maximum	23.13 $\pm$ 10.63	0.4	14	23.5	33.2	42.6
Mean	19.08 $\pm$ 9.98	-0.89	9.83	19.28	28.39	36.5
Minimum	14.12 $\pm$ 9.33	-7.6	6	14.2	22.4	32
Relative humidity (%)	31.82 $\pm$ 16.77	7.46	17.53	28.58	42.17	85.07
PM₁₀($\mu\text{g}/\text{m}^3$)	96.62 $\pm$ 39.74	31.78	69.40	86.55	112.70	364.44
NO₂ (ppb)	36.69 $\pm$ 9.07	15.49	28.72	37.26	43.34	67.27
SO₂ (ppb)	19.97 $\pm$ 6.44	9.31	14.99	18.58	23.34	50.13
O₃ (ppb)	25.03 $\pm$ 8.34	6.43	20.12	25.44	30.24	53.73

Table 2

Pearson's correlation coefficients of weather conditions and air pollutants in Tehran, Iran, 2013–2016.

	Mean Temperature	Minimum Temperature	Relative Humidity	PM10	NO ₂	SO ₂	O ₃
Maximum temperature	0.987	0.954	−0.816	−0.055	−0.14	−0.013	0.118
Mean Temperature			−0.810**	−0.048	−0.245**	−0.077	0.142**
Minimum Temperature			−0.750**	−0.030	−0.202**	−0.031	0.033
Relative Humidity				0.117*	0.114**	0.066	−0.210**
PM10					0.051	0.132**	−0.330**
NO ₂						−0.037	−0.057
SO ₂							0.176**

* P < 0.05.

** P < 0.001.

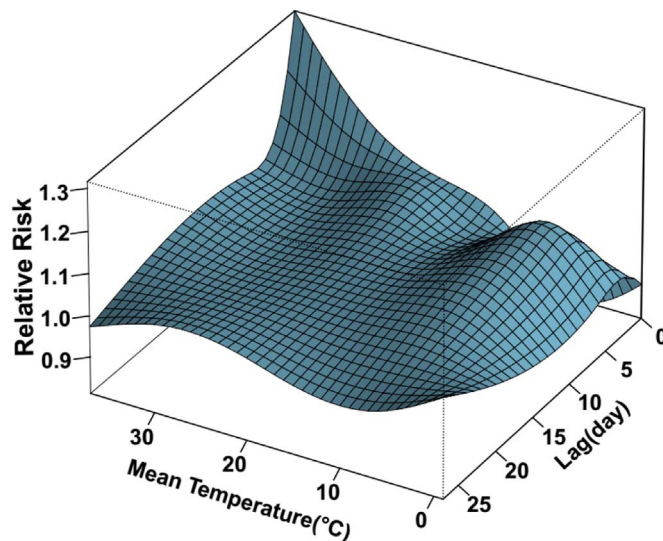


Fig. 1. Three-dimensional plot of the relationship between mean temperature and AMI admission over 27 lag days. The reference value was median temperature (19.3 °C).

about 8 days, whereas there was no statistically significant increased risk of AMI in females and those aged > 65 years old.

Table 3 shows the cumulative effects of hot and cold temperatures on overall, sex- and age-specific AMI admissions along 27 days lag. For hot effect, we calculated the cumulative effects by comparing 95th percentile of mean temperature (33.3 °C) with the 75th percentile of mean temperature (28.4 °C) along the lags. For the short lags (lag 0 and lag 0–3), the high temperatures were significantly associated with increased risk of AMI admission in the overall population, males, and people aged ≤ 65 years old, whereas for long lags (lag 0–27), high temperatures were only associated with increased risk of AMI admission in those aged > 65 years old. In general, people aged ≤ 65 years old and males were at higher risk than those aged > 65 years old and females respectively.

For cold effect, we calculated the cumulative effects by comparing 25th percentile of mean temperature (9.8 °C) with the 5th percentile of mean temperature (4.8 °C) along the lags. Generally, there were no significant increased risk of AMI admission in the overall population, females, people aged ≤ 65 years old, and those aged > 65 years old and only relative risk for males at lag 0–27 was statistically significant result (RR: 1.32, 95%CI: 1.05–1.66).

3.1. Sensitivity analysis

We changed the maximum lag from 14 to 30 days, the results of which did not change substantially compared to the maximum lag set to 27 days. We changed the window length of the calendar month in the case-crossover to 30, 28, and 21 days, and the estimated effects of mean temperature did not change. In addition, changing the df (3–7) for

relative humidity, PM10, SO₂, NO₂, and O₃ gave similar results. These results confirmed the robustness of the main effects of temperature on AMI admission against alternative models.

4. Discussion

In the present study, we examined the nonlinear and lagged effects of ambient temperature on AMI admission in Tehran, Iran, during the period March 21, 2013, to March 19, 2016. We identified a nonlinear relationship between mean temperature and AMI admissions. Our study also showed that both hot and cold temperatures had deleterious effects on AMI admission. Effects of high temperature appeared immediately on the current day and lasted for 3 days, whereas cold effects became apparent after 2 days and persisted for about 10 days. Moreover, the early acute effect of high temperature on AMI admission was followed by a deficit, which suggests evidence of a harvesting effect. We also observed that males and those aged ≤ 65 years old were more vulnerable to high temperatures.

Many previous studies have described a nonlinear U-, J-, or V-shaped relationship between ambient temperature and cardiovascular mortality (Breitner et al., 2014; Zhang et al., 2016; Yu et al., 2011; Huang et al., 2014), but few studies have specifically investigated the nonlinear effects of ambient temperature on AMI. In a review, Bhaskaran et al. found 16 studies that investigated temperature's short-term effects on AMI hospital admissions. Of these 16 studies, temperature's nonlinear effects on AMI were examined only in 6 studies (Bhaskaran et al., 2009). However, in line with our finding, several previous studies also reported a nonlinear relationship between temperature and AMI admission risk (Michelozzi et al., 2009; Lee et al., 2014; Dilaveris et al., 2006; Sharovsky et al., 2004; Enquesselassie et al., 1993). For instance, two studies from Australia and Brazil found a nonlinear U-shaped relationship between temperature and AMI admission when using quintiles of temperature (Enquesselassie et al., 1993; Sharovsky et al., 2004).

Our finding of deleterious effects of both hot and cold temperature on AMI admission has been reported by several authors (Wichmann et al., 2012b; Bhaskaran et al., 2010, 2012; Chang et al., 2004; Goggins et al., 2013; Bhaskaran et al., 2012). Bhaskaran et al. in their systematic review, concluded that both hot and cold temperatures had adverse effects on AMI hospital admissions (Bhaskaran et al., 2009). Dilaveris et al. reported a U-shaped minimum daily AMI deaths at 23.3 °C (Dilaveris et al., 2006). Similarly, an analysis in Sao Paulo, Brazil, found a significant adverse effect of both high and low daily temperatures on deaths due to MI (Sharovsky et al., 2004). Furthermore, our results are compatible with studies that examined the association between ambient temperature and cardiovascular mortality (Zhang et al., 2016; Guo et al., 2011; Bao et al., 2016). For example, an analysis in Tianjin, China, reported significant effects of both extreme cold and high temperatures' effects on cardiovascular mortality (Guo et al., 2011).

In this study, we found that the effect of hot temperatures on AMI admissions was acute and short term, while the cold effect was delayed about 2 days and persisted longer than the effect of hot temperatures. A similar pattern has been reported in many previous studies that

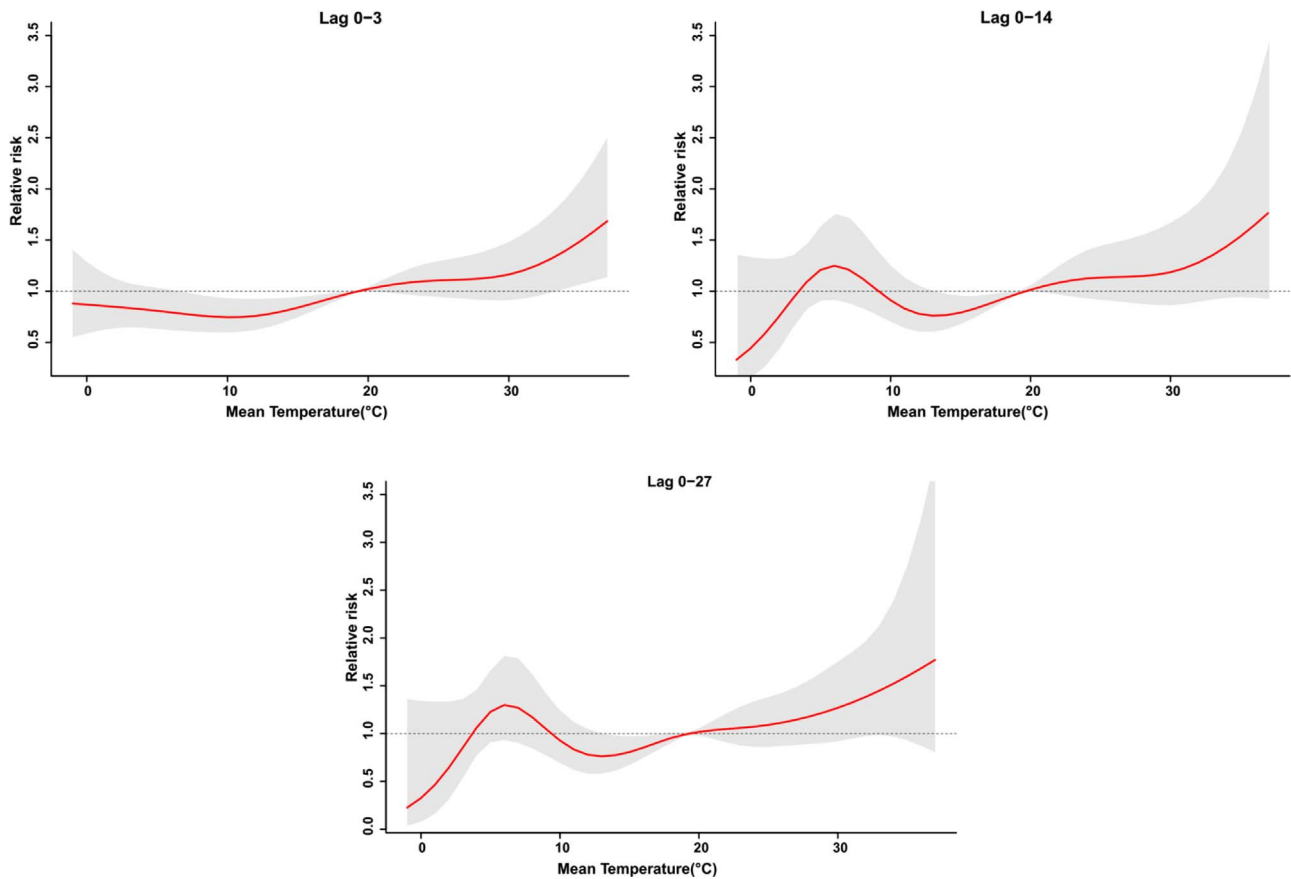


Fig. 2. The estimated cumulative effects of mean temperature ($^{\circ}\text{C}$) over lag days 0–27 on AMI admission at lag 0–3, lag 0–14, and lag 0–27, using a DLNM model with 5 df natural cubic spline for temperature and 4 df for lag. The reference value was median temperature (19.3°C). The red lines represent relative risks, and gray regions represent 95% confidence intervals.

examined the short-term effects of temperature on cardiovascular disease morbidity and mortality (Zhang et al., 2016; Guo et al., 2011; Yi and Chan, 2015; Tian et al., 2016; Schwartz et al., 2004; Muggeo and Hajat, 2009). For example, Tian et al. examined the nonlinear delayed relationship between ambient temperature and emergency

cardiovascular hospitalization and found significant positive effects of cold that were delayed for 2 days, and hot effect was acute on lag 0 day (Tian et al., 2016). In a study of 12 U.S. cities, Schwartz et al. consistently observed that the effects of hot temperatures on heart disease and AMI admissions appeared more immediately than the effects of

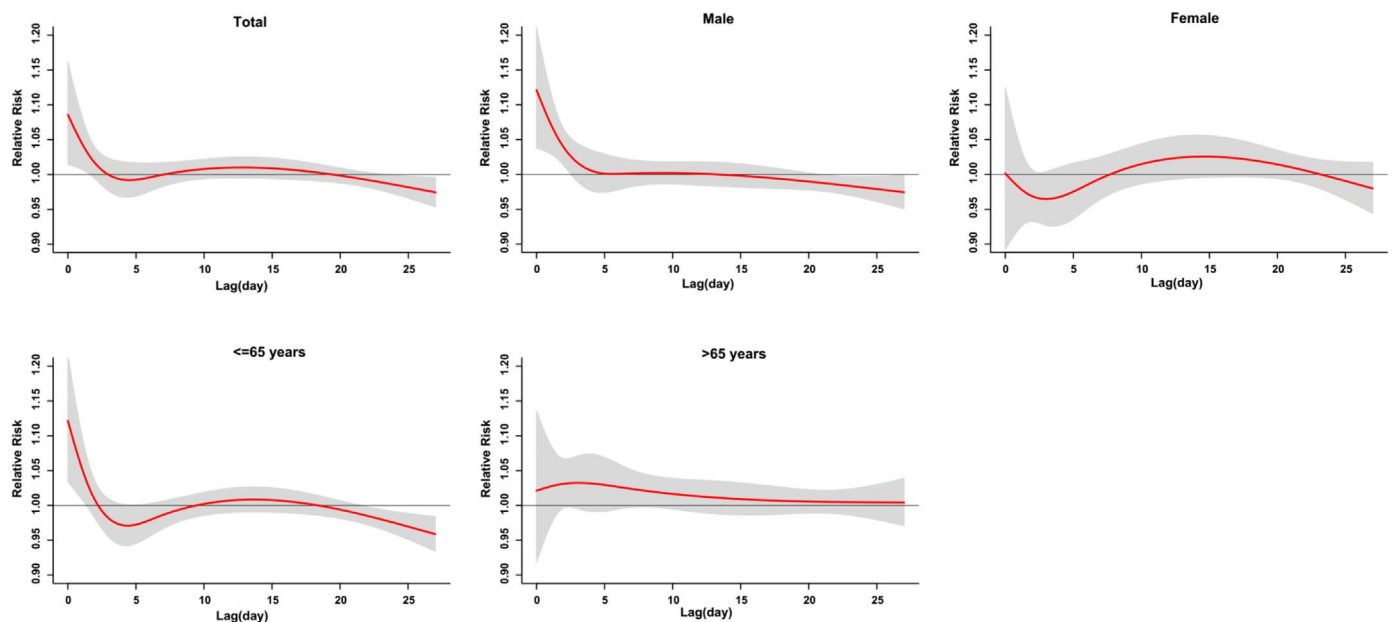


Fig. 3. The estimated effects of high temperature (33.3°C , 95th percentile of mean temperature) relative to 75th percentile of mean temperature (28.4°C) on AMI admissions by gender and age categories over 27 days of lag. The red lines represent relative risks, and gray regions represent 95% confidence intervals.

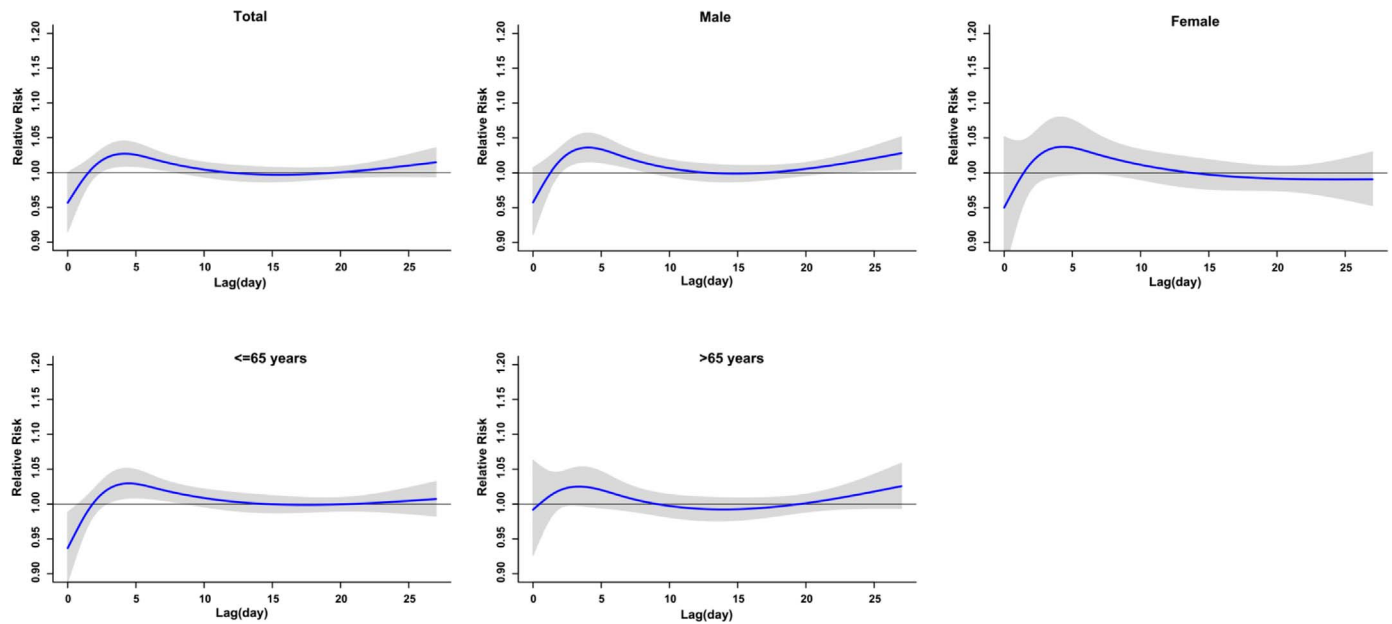


Fig. 4. The estimated effects of cold temperature (4.8 °C, 5th percentile of mean temperature) relative to the 25th percentile of mean temperature (9.8 °C) on AMI admissions by gender and age categories over 27 days of lag. The blue lines represent relative risks, and gray regions represent 95% confidence intervals.

cold temperatures (Schwartz et al., 2004). Furthermore, in a review of epidemiologic evidence on the relationship between ambient temperature and morbidity, Ye et al. found that the majority of studies have described acute and short-term detrimental effects of hot temperature and delayed and long-lasting effects of cold temperature (Ye et al., 2012).

Consistent with results of several mortality studies (Guo et al., 2011; Liu et al., 2011; Kalkstein and Greene, 1997; Muggeo and Hajat, 2009), our results revealed evidence of a harvesting effect of hot temperature during lag 3–9 days. Nevertheless, only a few studies have reported the presence of harvesting effect in morbidity studies. Schwartz et al. examined the effects of ambient temperature on hospital admissions for heart disease and myocardial infarction among individuals ≥ 65 years of age and found that initial positive effect of hot exposure at lag 0 was followed by a period of lower-than average admissions, which suggested evidence of a harvesting effect (Schwartz et al., 2004). Recently, Tian et al. also found that acute effect of hot temperatures on emergency hospital admissions for circulatory diseases on lag 0 day was

followed by harvesting on lag 2–4 (Tian et al., 2016).

We found that males and people aged ≤ 65 years old were more vulnerable to high temperatures. Previous studies that evaluated vulnerability to extreme temperatures by demographic characteristics, have reported inconsistent results. Wichmann et al. also reported that males and those aged 19–65 years old were at higher risk of AMI hospital admissions associated with extreme temperatures (Wichmann et al., 2012b). However, Kwon et al. reported that females and older age group had higher risks from hot and cold temperatures than males and younger age group respectively (Kwon et al., 2015). Higher vulnerability to high temperatures among males could be because men have a higher risk for developing CVD than females (Wichmann et al., 2012a). In addition, males and people aged ≤ 65 years contribute in more outdoor jobs and activities and are more likely to be exposed to high temperatures.

In our analysis, we chose 27 days as maximum lags to adequately capture the prolonged effect of cold temperature and potential harvesting effect of hot temperature on AMI admission. Since in our study

Table 3

The cumulative effects of cold and hot temperatures on AMI admission along the lag days.

Effect type	Lag(day)	Relative risk(95% CI)				
		Total	Male	Female	≤ 65 years	> 65
Hot effect	Lag 0	1.08 (1.01, 1.16)*	1.12 (1.04, 1.21)*	1.00 (0.89, 1.12)	1.12 (1.03, 1.22)*	1.02 (0.92, 1.13)
	Lag 0–1	1.13 (1.02, 1.26)*	1.20 (1.07, 1.35)*	0.98 (0.82, 1.17)	1.18 (1.04, 1.34)*	1.05 (0.89, 1.23)
	Lag 0–2	1.15 (1.02, 1.30)*	1.25 (1.10, 1.43)*	0.95 (0.78, 1.16)	1.19 (1.04, 1.37)*	1.08 (0.90, 1.30)
	Lag 0–3	1.15 (1.02, 1.30)*	1.27 (1.11, 1.46)*	0.92 (0.75, 1.13)	1.17 (1.01, 1.35)*	1.12 (0.93, 1.35)
	Lag 0–7	1.13 (0.98, 1.30)	1.28 (1.09, 1.50)*	0.85 (0.66, 1.09)	1.07 (0.90, 1.26)	1.25 (1.00, 1.54)*
	Lag 0–14	1.19 (1.00, 1.42)	1.29 (1.06, 1.58)*	0.95 (0.67, 1.35)	1.09 (0.88, 1.35)	1.38 (1.05, 1.82)*
	Lag 0–21	1.22 (0.99, 1.50)	1.23 (0.97, 1.57)	1.09 (0.70, 1.69)	1.09 (0.85, 1.40)	1.45 (1.05, 2.01)*
Cold effect	Lag 0–27	1.10 (0.89, 1.36)	1.09 (0.86, 1.39)	1.04 (0.67, 1.62)	0.92 (0.71, 1.19)	1.49 (1.07, 2.07)*
	Lag 0	0.96 (0.91, 1.00)	0.96 (0.91, 1.01)	0.95 (0.86, 1.05)	0.94 (0.89, 0.99)*	0.99 (0.92, 1.06)
	Lag 0–1	0.94 (0.88, 1.01)	0.95 (0.88, 1.03)	0.94 (0.80, 1.10)	0.91 (0.84, 0.99)	1.00 (0.90, 1.11)
	Lag 0–2	0.95 (0.88, 1.03)	0.97 (0.88, 1.06)	0.95 (0.79, 1.14)	0.92 (0.83, 1.01)	1.02 (0.90, 1.15)
	Lag 0–3	0.97 (0.90, 1.06)	0.99 (0.91, 1.10)	0.98 (0.80, 1.19)	0.94 (0.85, 1.03)	1.04 (0.92, 1.19)
	Lag 0–7	1.06 (0.96, 1.18)	1.12 (1.00, 1.26)	1.11 (0.87, 1.42)	1.04 (0.92, 1.17)	1.12 (0.95, 1.31)
	Lag 0–14	1.08 (0.95, 1.24)	1.16 (0.99, 1.35)	1.18 (0.87, 1.60)	1.09 (0.93, 1.28)	1.09 (0.88, 1.35)
	Lag 0–21	1.07 (0.91, 1.27)	1.18 (0.97, 1.43)	1.13 (0.79, 1.61)	1.08 (0.87, 1.33)	1.07 (0.82, 1.40)
	Lag 0–27	1.13 (0.93, 1.38)	1.32 (1.05, 1.66)*	1.07 (0.71, 1.61)	1.11 (0.88, 1.41)	1.18 (0.86, 1.62)

* $p < 0.05$.

hot effects occurred immediately followed with harvesting effect, whereas cold effects were delayed and persisted more than a week, using short lags could lead to overestimation of hot effects and underestimation of cold effects.

The adverse effects of high and cold temperatures on AMI admission can be explained by some biological mechanisms. During exposure to hot temperature, blood flow shifts away from body core to skin surface to cool the body (Kovats and Hajat, 2008, Wichmann et al., 2011) and cardiac output rises significantly due to vasodilation of blood vessels (González-Alonso, 2012). Prolonged heat exposure can lead to inadequate thermoregulation because of dehydration and salt depletion and may put stress on the cardiovascular and respiratory systems (Bouchama and Knochel, 2002; Basu, 2009). Additionally, high temperature is also associated with elevated plasma viscosity and serum cholesterol levels (Mcgeehin and Mirabelli, 2001), which may increase the risk of AMI admission.

On the other hand, exposure to cold is associated with rise in blood pressure, heart rate, and peripheral vasoconstriction, as well as thrombogenic factors, such as plasma viscosity, serum cholesterol levels, fibrinogen concentrations, platelet aggregation, and red blood cell count (Keatinge and Donaldson, 1994, Luo et al., 2012, Cheng and Su, 2010, Keatinge et al., 1984). These could all be risk factors for cardiovascular disease and can precipitate AMI, especially among susceptible people.

5. Strengths and limitations

To the best of our knowledge, the present study is the first study that used a case-crossover design jointly with DLNM to evaluate both hot and cold effects on AMI admissions in Tehran, Iran. By using this advanced statistical approach, we were able to examine both the non-linear and the lagged effects of temperature simultaneously. Another strength of the present study was that unlike most of other studies, we consider potential confounding effects of air pollution in our analyses.

Inevitably, this study had several limitations. First, as with all ecological time-series studies, we obtained temperature, humidity, and air pollution data from fixed monitoring stations rather than measures of individual exposure, which may lead to some degree of measurement error (i.e. underestimation of impact of temperature on AMI admission). Second, we did not consider preexisting disease or comorbidities, socioeconomic status, income, education, and access to air conditioning. Estimated effects of temperature on AMI admission may have been influenced by such factors. Finally, we analyzed only data from one city in Iran; therefore, the generalizability of the findings to other places or to rural areas is questionable.

6. Conclusions

This is the first study to investigate temperature's short-term effects on AMI admissions in Tehran, Iran. We observed a nonlinear relationship between mean temperature and AMI admissions. Both hot and cold temperatures had a deleterious effect on AMI admission. Hot effects were acute and short-term, whereas cold effects were delayed and persisted longer than hot effects. Males and those aged ≤ 65 years old were more vulnerable to high temperatures. These findings indicate that ambient temperature is an important risk factor for AMI hospitalizations, and preventive and intervention strategies should be established to reduce adverse health effects associated with extreme temperatures.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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